THE MOTOR UNIT: REVISITED*

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IN 1925 Sir Charles Sherrington[1] and Liddel and Sherrington[2] introduced the term "motor unit" to the physiological vocabulary. Sherrington's definition still defies semantic improvement: "The term 'motor unit' includes, together with the muscle fibers innervated by the unit, the whole axon of the motoneuron from its hillock in the perikaryon down to its terminals in the muscle." He also stated that "For the motor unit the 'all-or-none' principle of reaction is accepted..." and "that the unit contains further an 'all-or-none' effector in the muscle fiber itself...."

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The number of motor units in a muscle varies with its size and function; most human muscles contain several hundred. The number of muscle fibers in the motor unit varies and, therefore, the muscle's capacity to generate power also varies (from 80 to 60 gm.).

The number of muscle fibers innervated by a single axon ranges widely, from two or three (laryngeal) to several thousand (quadriceps). As early as 1863 Tergast[3] reported on nerve and muscle counts; his values erred because afferents or gamma fibers were not understood, but he did make the important observation that the external rectus muscle of the eye of the sheep had a ratio of nerve to muscle fiber of 1:3. This proportional statement is known as the innervation ratio; its accuracy requires consideration in the calculation that approximately 50% of the muscle nerves are efferents. In general, a relation exists between the required finesse of movement and the innervation ratio: the more finesse of movement, the

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lower the ratio; for example, eye muscles, associated with fine, rapid movements, show a low ratio, while the gross quadriceps muscle has a high ratio.

There has been little dispute that muscle fibers belonging to a single motor unit are not confined to a single muscle fascicle and that considerable interlacing occurs. This is important to note in assuring proper sampling of a muscle during an electromyographic examination. There is, however, considerable controversy regarding the finer distribution of the muscle fibers of the motor unit. Buchthal and his co-workers[4] postulated the existence of clumps of eight to 12 fibers in what they called subunits, basing the idea on light microscopic observations of persisting groups of muscle fibers in the atrophic muscle of patients with chronic motoneuron disease. This concept has been abandoned because of several precise observations:

1) Microscopic studies in other animals revealed no evidence of subunit grouping (Forbes-Morris[5]).

2) The original, elegant studies by Edström and Kugelberg,[6] in which single fibers of the ventral root supplying a muscle were isolated and then repetitively stimulated electrically at tetanic frequencies, showed the following result: The muscle was immediately excised, frozen, and stained for glycogen with Schiff's PAS stain. It was assumed that the tetany exhausted the cell glycogen so that the unstained cells represented a distribution from the single axon of the motor unit. It was observed that the fibers from a single unit were rarely contiguous and that territories of different motor units overlapped considerably. This normal scatter was no longer evident in studies carried out after transection and reunion of the nerve. Under these circumstances a clustering of enzymatically similar muscle fibers was noted; this has been referred to as a type grouping. This distribution generally is interpreted as evidence of reinnervation following subterminal sprouting from intact motoneuron fibers. Usually, the collaterization process is localized, but it is evident that the reinnervated fibers assume the metabolic characteristics of the donor motoneuron. The electromyographic counterpart of this process of increased fiber count and density is increased amplitude of motor-unit potential.

3) Final evidence against the subunit concept was provided by Ekstedt[7] and his co-workers, who used special electrodes and techniques to demonstrate conclusively that the spike potential was generated by single muscle fibers and that no synchronization of the electrical activity of the single

STAINING CHARACTERISTICS OF TYPE I AND TYPE II MUSCLE FIBERS

Stain for:	*Type I*	*Type II*
Myofibrillar adenosine triphosphatase at *p*H 9.4	Low	High
Glycogen	Low	High
Oxidative enzymes (dehydrogenases)	High	Low

fibers derived from a single motor unit occurred, which would have to be the case if the theoretical subunit did exist.

Abandonment of the subunit concept, however, does not invalidate the Copenhagen investigator's contributions in the study of the motor-unit territory.[4] This measurement was introduced by Fritz Buchthal and his co-workers, who used a multielectrode with 14 1.5 to 2 mm. leads to scan the entire depth of a muscle (20 to 30 mm.), and to measure the geographical area of a muscle potential with a spike of at least 5 μV in amplitude and a rise time of less than 200 μsec. They showed that the territory was circular and varied from 5 to 11 mm. (biceps brachii = 5 mm.), with a fourfold variation from unit to unit within a given muscle. Characteristically, the muscle territory is enlarged in neuropathic diseases and contracted in primary myopathies.

Some of the metabolic attributes of muscle fibers now can be differentiated by enzymatic histochemical studies. In humans, two major categories of fibers, Type I and Type II, may be identified by staining for myofibrillar ATPase at *p*H 9.4.[8] The accompanying table summarizes the difference between these two types. Type I fibers, poor in this enzyme, stain lightly while Type II stain heavily. The soleus muscle (slow-twitch) is a good example of Type I, while the gastrocnemius muscle (fast-twitch) exemplifies Type II. When these fiber types are histochemically stained for oxidative enzymes (e.g., NADH-reduced diphosphopyridine nucleotide, a flavoprotein also referred to as NADH diaphorase), the characteristic light and dark colorations are reversed. Type I fibers have a relatively poor content of glycogen compared with Type II fibers and stain poorly with Schiff's PAS reagent. Type II fibers often show a strong pink color.

It is now accepted that the alpha motoneurons of the spinal cord are also type specific, and that Type I motoneuron and its Type I axon innervate Type I muscle fibers, a specificity apparently imposed on fibers reinnervated via sprouting.

Electrophysiology of the Motor Unit

When a motoneuron discharges volitionally or reflexly for nearly all purposes it may be assumed that an all-or-none excitation of the muscle fibers of the motor unit occurs. Some variation in the diameter of terminal arborizations of the axon, slight differences in conduction velocity, and some special dispersion of motor endplates are associated with slight synchrony in the action potential of single muscle fibers. Because electromyography is carried out in a volume conductor,* voltages generated by single fibers and overlapping motor units algebraically sum to produce an essentially smooth motor-unit action potential. Indices describing this action potential are subject to variations related to the type and size of recording electrodes, but most published papers are based on observations from electrodes with a single core concentric needle.

The configuration of this action potential usually is predictably triphasic when recording in a volume conductor; a sharp positive to negative spike is preceded and followed by a smaller positive component. Distant fibers contribute positive components and the spike is caused by voltages generated by the few muscle fibers subtending the recording electrode's exposed tip. It is estimated that the motor-unit territory must allow for 10 to 25% overlapping units; the single motor-unit action potential which is recorded represents many contributions of the motor unit to the shape through the temporal and spatial dispersion of their spike components. In normal muscles 3% of the motor-unit action potentials show a late spike approximately 9 to 16 msec. after the main components.[10] Late spike components are not infrequent in disease,[12] especially with good collateral reinnervation (e.g., Kugelberg-Welander syndrome).

Amplitudes and durations vary within a single muscle and from muscle to muscle. It is necessary, therefore, to sample at least 20 to 30 motor-unit action potentials from each muscle for valid measurement. The amplitude of the single motor-unit action potential is very unreliable; from 300 μV to 5 mV is a representative normal range. The distance between the center of the generated voltages and the recording electrodes is a major determinant in the amplitude of the spike of the motor-unit action potential because of the volume-conductor effect. Displacement of 0.12 mm. results in an attenuation of 50%, at 0.38 mm. the attenuation is 90%, and at 1.0 mm. the reduction in amplitude is 99%![12] Above 5 mV units are defined as

*A volume conductor refers to the fact that the human body acts as an electrolytic solution and conducts electrical current in three planes away from the point of generation of the voltage.

giant or hypertrophied. Measurement of a unit with a spike-rise time of more than 150 to 200 μsec. or with a voltage below 50 μV is unreliable.

The amplitude reflects the number of muscle fibers in the unit, although it is probably more correct to say that it reflects fiber density. In motoneuronal disease, if collateral reinnervation is great the motor-unit potential characteristically is hypertrophied and histochemically characterized by type grouping.

The total duration of the motor-unit action potential is mostly attributable to the slow positive components before and after the spike caused by temporal dispersion of arrival times of potentials from fibers innervated at the extreme widths of the zone of innervation. When distant fibers are destroyed, as in muscular dystrophy, positive portions are wiped out, leaving motor-unit action potentials of characteristically short duration.

The duration of the motor-unit action potential varies with age. For the biceps brachii at three years the duration is 7.3 msec. and at age 75 it is 12.8 msec. Duration also varies from muscle to muscle—the facial has a duration of approximately 2 to 4 msec., and the quadriceps has a duration of 12 msec.

Relating muscle-fiber type to characteristics of motor-unit potentials has been attempted. Warmolts and Engel[13] carried out open-biopsy electromyography with concentric needle electrodes and compared histochemical features with the electromyogram. The patients all had low-grade motor neuropathies with high-density homogenous populations of either Type I or Type II muscle fibers. The following characteristics were observed:

1) Patients with a preponderance of Type I muscle fibers had high-amplitude motor-unit action potentials which had a low frequency of from 50 to 10/sec. and were easily recruited with graded effort.

2) Patients with a preponderance of Type II muscle fibers had recruitment only with rapid, vigorous effort and showed bursts of high-frequency action potentials of at least 15/sec. They also showed that in a patient with myotonic dystrophy with the characteristic selective Type I atrophy the motor-unit action potentials were recruited by graded effort but were considerably smaller in amplitude than in the normal controls.

Buchthal and Schmalbruch[14] measured the contraction time of the slow soleus muscle and the fast-twitch lateral head of the triceps in man in an attempt to correlate fiber types and the electromyogram. The average soleus rise time was 190 $\pm$ μsec. and for the triceps 107 $\pm$ 4 μsec.

Recordings were carried out with concentric needle electrodes which had tips of 0.015 mm. diameter (normal 0.075) and a rapid sweep speed of 0.1 msec./cm. A delay line was used. In patients with myopathy the spectrum shifted to slower rise times.

Engel[15] has compared motor units to trees. The soma of the motoneuron is likened to the base, axons would be the trunk and boughs, and the individual muscle fibers would be leaves. A tree may be affected entirely *(in toto)* or partially *(ex parte)*.

All *in toto* motor-unit disorders are neuropathies. *Ex parte* motor-unit disorders may be either neuropathic, e.g., toxic-impaired axoplasmic flow, or myopathic, in which some fibers of the motor-unit degenerate because of postjunctional disease while the nerve is not affected.

In each instance muscle fibers degenerate and reduce the motor-unit complement, resulting in an electromyogram showing brief, small amplitude and excessively abundant potentials which, therefore, are pathognomic of neither myopathy or neuropathy.

Estimating the Number of Motor Units within a Muscle

Accurate assessment of the number of active motor units within a muscle would be of inestimable value in investigating and detecting neuromuscular diseases. Procedures based on the analysis of the interference pattern, although presenting valuable information, provide only approximations of the intact motor unit content.

Gradation of muscular activity is accomplished by recruitment of additional motor-units and changing the firing rate of the motor unit. With beginning weak contractions, small motor-unit action potentials are mobilized at a rate of 5 to 15/sec. With increased effort comes active recruitment of motor-unit potentials, recognized by their variations in amplitude and configuration, and frequently larger than the first group. Firing rates increase into the range of 50/sec.

When the electromyogram in a normal subject is recorded continuously at slow sweep speeds (10 msec./cm.) the tracing is termed an interference pattern. At minimal effort, single motor-unit action potentials can be identified; this is known as a single unit pattern. At maximum effort no base line is discernible because there are many overlapping, rapidly firing units; this is known as total interference. These patterns of recruitment are useful in differentiating between primary myopathy and neuropathy.

A more recent method to evaluate the content and functional status of motor units, although restricted to particular muscles, attempts to provide an estimate of the number of functioning motor units.[16] The principle is simple: the amplitude of the action potential generated by a single motor unit of average size divided into the potential sum of all the motor units in the muscle will equal the number of motor units within the muscle. In practice, the procedure is carried out in a quantified manner: to grade the strength of an electrical stimulus applied to an appropriate motor nerve carefully, to recruit successive single motor units, and to calculate the mean motor-unit potential amplitude. Response of the total population of units is evoked by maximal stimulus to the nerve.

Most observations were made with the extensor digitorum brevis muscle. A pair of recording electrodes was placed to cover the endplate zone completely. The stimulus, rectangular voltage pulses of 50 μsec. duration, was increased gradually from a subthreshold value until 11 increments in muscle response were recorded. Intermediate responses were never observed; therefore, each increment was attributed to activation of an additional motor unit. The muscular response after stimulation of the supramaximal motor nerve also was recorded as an example. For a normal subject, e.g., if the mean motor-unit potential was 40 μV and the total muscle response was 9 mV, motor units were calculated to number 200.

The method, a gross investigation of a sample of units representative of the entire population, is difficult, and some of the increments may not correspond to additional single-unit responses. In spite of these reservations, McComas et al. found that the reproducibility of results in any subject, e.g., if the mean motor-unit potential was 40 μV and the total well with calculations based on counts of axons in postmortem specimens of the peroneal nerve.

The procedure subsequently was applied by McComas and his colleagues to patients with various neuromuscular disorders. The results, particularly in the different forms of muscular dystrophy, and the conclusions drawn therefrom did not conform to classical concepts, and hence became highly controversial. These investigators reported a reduction in the number of functioning motor units of the extensor digitorum brevis muscle in Duchenne muscular dystrophy, myotonic dystrophy, limb-girdle and facioscapulohumeral dystrophies, Kugelberg-Welander syndrome, motoneural disease, atrophy after motoneural lesions, McArdle's disease, and thyrotoxicosis. Likewise, progressive loss of functioning motor units

was identified in healthy individuals more than 60 years old. Extending the study to other muscles, the same investigators found a selective loss of motor units in the thenar, hypothenar, and soleus muscles of patients with muscular dystrophy. They eliminated the possibility that this could have resulted from nerve trauma because there was no evidence of sensory axon involvement in the median, ulnar, and sural nerves. It was noted, however, that in any one patient the extensor digitorum brevis muscles were likely to be more involved than the thenar or hypothenar muscles.

To explain these observations, McComas et al. introduced the concept of "sick" motoneurons[17] and described three stages of motoneural function: healthy, sick, and dead. A motoneuron was regarded as healthy if it conducted impulses at normal rates along the axon, transmitted excitation effectively across the neuromuscular junctions, and maintained all the muscle fibers of the motor unit in a healthy condition. A motoneuron which was sick as a result of disease had difficulty maintaining satisfactory synaptic connections with muscle fibers. Thus, conduction velocity along the axon can be normal, while the ability to acquire previously denervated muscle fibers is impaired. Dead motoneurons are those which have ceased to exert any influence on muscle fibers.

In Duchenne and myotonic dystrophy the surviving motoneurons were regarded as sick because they have ceased to exert any influence on the muscle fibers, and the relatively normal sizes of their units indicated that the cells had failed to innervate the muscle fibers relinquished by the dead motoneurons. In limb-girdle and facioscapulohumeral dystrophies a neurogenic process was also implicated because the presence of enlarged motor units meant that potentially healthy muscle fibers had lost their original nerve supply and had been reinnervated by healthy neurons. They therefore suggest that diseases long considered primary disorders of muscle actually may result from abnormal motoneuron function.

This proposal, representing the strongest support for the neurogenic hypothesis of muscular disease, has not received wide acceptance. The method has been criticized on the grounds that the noise level of the recording system was high enough to obscure motor-unit potentials of small amplitude, which are expected in the dystrophies and are indicated by the electromyographic findings of small-amplitude and short-duration motor-unit potentials. Another criticism was based on findings in the thenar and extensor digitorum brevis muscles that demonstrated the presence of single motor units much larger than those few close to the motor

threshold on which the average potential is based. This suggests that estimates based on the average potential of the first few units excited above the motor threshold may not be valid and may overestimate the true motor-unit population.

Independent investigations using variations of McComas' procedures have disagreed with the original findings. In one recent study[18] estimations of the number and size of motor units in the extensor digitorum brevis muscle showed no significant difference between patients with Duchenne muscular dystrophy and controls, while the size of the motor-unit action potentials were significantly reduced in the patients. Similarly, the same authors found no loss of functional motor units in limb-girdle muscular dystrophy, but found a decreased number in chronic muscular atrophy.

New results recently were reported by Ballantyne and Hansen,[19,20] whose novel system utilized on-line computer analysis. Their procedure resembled that of McComas et al., except that data was processed on-line by computer. Successive motor units recruited singly by application of finely graded stimuli to the anterior tibial nerve were displayed; these were recognized by an operator who then instructed the computer to store the potential. In this manner electrical responses of the first evoked motor unit; the first and second; the first, second, and third; and so on (up to 15 memory items) were stored sequentially in the computer. Finally, the supramaximally evoked muscular action potential was sampled and stored. The absolute area of the potential in each memory store was derived and the number of motor units was calculated by dividing the average absolute area into the absolute area of the supramaximally evoked muscular action potential. This differs from the procedure of McComas et al. where peak-to-peak amplitudes of the evoked potentials were measured to calculate the number of motor units. Similar on-line computer analysis can isolate the electrical responses of individual motor units from the muscle compound action potential (by serial subtraction of the memory stores) and can measure latencies, amplitudes, and durations. Ballantyne and Hansen found that the number of motor units in the extensor digitorum brevis muscle of patients with myasthenia gravis and Duchenne, limb-girdle, and facioscapulohumeral muscular dystrophies were within normal ranges, but were reduced significantly in patients with myotonic muscular dystrophy. They prefer their computer-assisted method to the amplitude method of McComas et al. and question the validity of the latter's results and concepts.

The supposed neurogenic basis for neuromuscular disease seems to be losing support; for example, considerable difficulty exists with accepting McArdle's disease as a neurogenic entity. Recently, Law, Cosmos, Butler, and McComas[21] demonstrated that reinnervation of healthy murine limb muscles with nerves from genetically determined dystrophic mice did not result in changes characteristic of muscular dystrophy.

The spectrum of neuromuscular diseases can be viewed as dysfunctions of the motor unit. This functional concept is certainly not new, but remains vigorous and dynamic.

REFERENCES

1. Sherrington, C. S.: Remarks on some aspects of reflex inhibition. *Proc. R. Soc. Med. 97B:*519-45, 1925.
2. Liddell, E. G. T. and Sherrington, C. S.: Recruitment and some other features of reflex inhibition. *Proc. R. Soc. Med. 97B:*488-518, 1925.
3. Tergast, P.: Ueber das Verhältniss von nerve und muskel. *Arch. Mikr. Anat. 9:*36-46, 1873.
4. Buchthal, F., Guld, C., and Rosenfalck, P.: Volume conduction of the spike of the motor unit potential investigated with a new type of multielectrode. *Acta Physiol. Scand. 38:*331-54, 1957.
5. Norris, F. H. and Irwin, R. L.: Motor unit area in rat muscle. *Am. J. Physiol. 200:*944-46, 1961.
6. Edström, L. and Kugelberg, E.: Histochemical composition, distribution of fibres and fatiguability of single motor units. Anterior tibial muscle of the rat. *J. Neurol. Neurosurg. Psychiatry 31:*424-33, 1968.
7. Ekstedt, J.: Human single muscle fiber action potentials. *Acta Physiol. Scand.* (Suppl.) *61:*1-96, 1964.
8. Engel, W. K.: The essentiality of histo- and cytochemical studies of skeletal muscle in the investigation of neuromuscular disease. *Neurology 12:*778-84, 1962.
9. Henneman, E., Somjen, G., and Carpenter, D.: Excitability and inhibitability of motor neurons of different sizes. *J. Neurophysiol. 28:*599-620, 1965.
10. Buchthal, F. and Rosenfalck, P.: On the Structure of Motor Units. In: *New Developments in Electromyography and Clinical Neurophysiology,* Desmedt, J. E., editor. Basel, Karger, 1973, vol. 1, pp. 71-85.
11. Borenstein, S. and Desmedt, M. J. E.: Electromyographical Signs of Collateral Reinnervation. In: *New Developments in Electromyography and Clinical Neurophysiology,* Desmedt, J. E., editor. Basel, Karger, 1973, vol. 1, pp. 130-40.
12. Rosenfalck, P.: Intra- and extracellular potential fields of active nerve and muscle fibres. *Acta Physiol. Scand.* (Suppl.) *75:*1-168, 1969.
13. Warmolts, J. R. and Engel, W. K.: Open-biopsy electromyography. Correlation of motor unit behavior with histochemical muscle fiber type in human limb muscle. *Arch. Neurol. 27:*512-17, 1972.
14. Buchthal, F. and Schmalbruch, H.: Contraction times and fibre types in intact human muscle. *Acta Physiol. Scand. 79:*435-52, 1970.
15. Engel, W. K. and Warmolts, J. R.: The Motor Unit. In: *New Developments in Electromyography and Clinical Neurophysiology,* Desmedt, J. E., editor. Basel, Karger, 1973, vol. 1, pp. 141-77.
16. McComas, A. J., Fawcett, P. R. W., Campbell, M. J., and Sica, R. E. P.: Electrophysiological estimation of the number of motor units within a human muscle. *J. Neurol. Neurosurg.*

Psychiatry 34:121-31, 1971.
17. McComas, A. J., Sica, R. E. P., Upton, A. R. M., and Petito, F.: Sick motoneurons and muscle disease. *Ann. N.Y. Acad. Sci. 228*:261-79, 1974.
18. Panayiotopoulos, C. P., Scarpalezoa, S., and Papapetropoulos, T.: Electrophysiological estimation of motor units in Duchenne muscular dystrophy. *J. Neurol. Sci. 23*:89-98, 1974.
19. Ballantyne, J. P. and Hansen, S.: A new method for the estimation of the number of motor units in a muscle. *J. Neurol. Neurosurg. Psychiatry 37*:907-15, 1974.
20. Ballantyne, J. P. and Hansen, S.: New method for the estimation of the number of motor units in a muscle. *J. Neurol., Neurosurg. Psychiatry 37*: 1195-1201, 1974.
21. Law, P. K., Cosmos, E., Butler, J., and McComas, A. J.: The absence of dystrophic characteristics in normal muscles successfully cross-reinnervated by nerves of dystrophic genotype: Physiological and cytochemical study of crossed solei of normal and dystrophic parabiotic mice. *Exp. Neurol. 51*:1-21, 1976.